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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,867	02/04/2002	Halle Morton	999710000008	3108

7590 02/01/2006

EXAMINER
SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
1647	

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DATE MAILED: 02/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,867	MORTON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11 and 25-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-11 and 25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response Applicants response filed 10/27/2005. Claims 1, 3-11 and 25 have been amended. Claims 26-36 have been added. Claims 2 and 12-24 are cancelled. Thus, claims 1, 3-11 and 25-36 are pending and is the subject of this action.

2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

3. The Applicants have submitted a declaration under 37 C.F.R. 132, which has been fully considered.

Claim Rejections - 35 USC § 103, maintained

4. The rejection of claims 1, 3-11 and 25 under 103(a) as unpatentable over Morton et al. (WO 95/15338) in view of the M.S. study (Neurology, 1993) is maintained for reasons of record in the Office Actions dated 5 August 2003, 5 October 2004 and 27 April 2005 and is applied to new claims 26-36.

Applicants have amended claim 1 to require treating an active case of multiple sclerosis by administering cpn10 and IFN-β, wherein the therapeutic effect of administering cpn10 and IFN-β together is synergistically improved compared to therapeutic effect of administering the same equivalent amount cpn 10 or IFN-β alone. Applicants assert that neither Morton reference nor the MS study, nor combination thereof, teaches or suggests that combined cpn 10 and IFN-β treatment display a "markedly improved ability" to treat MS or delay relapse following cessation of other treatments. Further it is asserted that there is no express or inherent motivation in the

cited or prior art to combine these two references. Further it is stated that the prior art actually taught away from using cpn10 and IFN-β in combination therapy (see page 10, of the 10/27/2005 response). Applicant argues that there is no motivation in the prior art to achieve for this greater effect. Applicant further argues that this effect is unexpected from the teachings of the prior art.

Applicants also assert that based on the expert declaration provided by Dr. Barbara Johnson under Rule 132, cpn10 and IFN-β act via different biological mechanisms to reduce MS symptoms and decrease relapse frequency. It is also asserted that at the time of this invention a skilled artisan would not have been able to predict an improved therapeutic effect upon the combined administration of cpn10 and IFN-β, particularly when using a dosage of IFN-β that will not cause clinically significant IFN-β induced side effects. In addition, Applicants claim that Dr. Johnson's declaration notes that the art implicitly taught away from the present invention by teaching that cpn10 and IFN-β have same biological mechanism of action.

In addition, Applicants also assert that the data present on Figures 8, 9 and Table 4 together demonstrate a statistically significant difference between administering cpn10 and IFN-β alone versus combined cpn10 and IFN-β administration (see page 11 of the response filed 10/27/2005). Applicants also contend that Dr. Johnson declares that invention achieves beneficial and synergistic result by using doses of each agent used alone. Applicants' arguments have been fully considered but have not been found to be persuasive.

While Applicants are correct in asserting that the prior art does not disclose the administration of cpn10 and IFN-β together, as disclosed previously in the Office Action dated 5 August 2003 (pages 4-5), *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

"It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art".

Although, Applicants recite that the therapeutic effect of administering cpn10 and IFN-β together is synergistically improved compared to therapeutic effect of administering the same equivalent amount cpn 10 or IFN-β alone, the evidence presented in Figures 8, 9 and Table 4 does not support this assertion. Figures 8 and 9, which are the two figures that compare combinations to individual administration, do not indicate that there is any unexpected benefit from this combination. Figure 8 shows an uneven progression with substantial overlap in the methods of treatment. Figure 9 shows a very modest difference. In addition, the mean disability score for the primary attack is reported on Table 4 to be 14.1 ± 2.3 (cpn10 alone), 17.4 ± 2.5 (IFN-β alone) and 13.6 ± 2.1 (cpn10 and IFN-β together). Similarly, the mean disability score for the "period of relapse" is reported on Table 4 to be 24.6 ± 8.2 (cpn10 alone), 27.1 ± 8.5 (IFN-β alone) and 17.9 ± 10.9 (cpn10 and IFN-β together). The artisan would expect at least an additive effect but the data shows very little advantage to the combination. Specifically, the co administration data appears to be statistically not significant

compared to cpm or IFN-β alone. There is no evidence of a synergistic effect. Thus there is no teaching of a result that would be unexpected from the combination of two agents that are useful for the same purpose, which combination is itself *prima facie* obvious for the reasons set forth in the previous office action(s).

Contrary to Dr. Johnson's declaration that the invention achieves the beneficial and synergistic result by using doses of each agent lower that would have been regarded as optimal dose for each agent used alone (Paragraph 13 of the declaration). It is argued that 2.5 μg of cpm10 administration in one aspect of the methods of the invention can be considered a suboptimal dose (because the Morton reference discloses the administration of 15μg of cpm10 to a mouse on page 21, line 23). However, the 2.5 μg of cpm10 administered to a 40g mouse (average adult mouse weight) in Example 6, is actually about 62.5 μg/kg body weight, which has been previously disclosed on page 27, lines 14-15 of Morton et al. (WO 95/15338). Furthermore, the administration 5000 IU of IFN-β in example 6, is also considered a lower dose based on the teaching of Yu et al. (1996). However, it is noted that the Office did not rely on this reference for its 103(a) rejection of record. In addition, claims 10, 11, 35 recite administering IFN-β in the range of 1 to 10 MIU, which was clearly taught by MS study (1.6 to 8 MIU). The administration of 5000 IU to 40 mg mouse is equivalent to 125 MIU, which is much higher than the contemplated dose. With respect to Applicants claim that Dr. Johnson's declaration notes that the art (Jeffery et al., 2004) taught away from the present invention by "the agent added to the primary therapy may have no effect, or, worse, may antagonize the effect of the primary agent". It also goes

on to say that in many instances whilst one may assume that the combination of two agents may have a beneficial effect, the opposite may be true. However, the complete reading of the article does teach away from combination therapy and suggests that studies are needed to address the question of whether there is an additive or synergistic effect and to address the long-term safety of the combination.

Although, Applicants claimed *prima facie* case of obviousness is established only when the teaching from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art and that art must suggest how to apply their teaching to the specifically claimed invention, as indicated previously *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) it is noted that "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art". Thus Applicant's specification fails to distinguish the invention from what would be prima facie obvious from the teachings of Morton et al. and the M.S. Project.

Applicants further assert that they have submitted sufficient evidence including Dr. Johnson's declaration, to indicate that there was a long-felt need for an invention such as that claimed in this application. However, declaration under 37 CFR 1.132 is insufficient to overcome the obviousness rejection, because there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem.

Specifically data shows very little advantage to the combination therapy to that of administering cpm or IFN-β alone as argued above.

Claim Rejections - 35 USC § 112, first paragraph (withdrawn)

5. The rejection of claims 1 and 3-7 under 35 U.S. C 112, first paragraph lacking in enabling disclosure for treatment MS using suboptimal levels cpm or IFN-β is withdrawn because Applicants have amended the claims to remove references to suboptimal doses.

6. The rejection of claim 2 under 35 U.S. C 112, first paragraph lacking in enabling disclosure for prevention of relapse is withdrawn because Applicants have cancelled the claim.

Claim Rejections - 35 USC § 112, second paragraph (withdrawn)

7. The rejection of claim 1-7 under 35 U.S.C 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim subject matter which applicant regards as invention is withdrawn because of Applicants have amended the claims to remove references to suboptimal doses.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

8. Claims 1, 3-11 and 25-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8a. Claims 1 and 33-36 are rejected as vague and indefinite for reciting the term "equivalent amount" is not defined in the specification. The artisan would be unable to

determine what amounts Applicants intended the claims to encompass. Claims 3-11,and 27-32 are rejected insofar as they are dependent on rejected claim 1.

8b. Claims 1 and 33-36 are rejected as vague and indefinite for reciting the term "active case" is not defined in the specification. Claims 3-11 are rejected insofar as they are dependent on rejected claim 1.

8c. Claims 25, 31 and 32 are also rejected as vague and indefinite for reciting the phrase "clinically significant IFN-β-induced side effects in the individual " is not defined in the specification. Claims 27-30 are rejected insofar as they are dependent on rejected claim 25.

8d. Claims 26 and 32 are rejected as vague and indefinite. In part (a) it is recited that two pharmaceutical compositions each comprising cpn10 or IFN-β meaning that,that both compositions can comprise one or the other. Claims 27-31 and 33-36 are rejected insofar as they are dependent on rejected claim 26. It is suggested that Applicants reword the claims as following "wherein one composition comprises cpn10 and the other comprises IFN-β" to obviate the rejection.

8e. Claim 28 is rejected as vague and indefinite for reciting the phrase "cpn10 and IFN-β, or cpn10 or IFN-β is provided in a separate container " because it is unclear how both cpn10 and IFN-β can be in separate containers? If cpn10 and IFN-β are together they cannot be in separate containers also. Clarification is required.

9. Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The specification as originally filed does not provide support the newly added limitation of "about" on claims 8-11. Applicant is required to cancel the new matter in the reply to this Office Action.

10. Claims 6 and 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of cpn 10 and IFN-β for the treatment of MS in liquid or solution form, does not reasonably provide enablement for treatment MS using tablet or capsule form. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Both the specification and the prior art teach that IFN-β and cpn 10 can be used to treat M.S by administering the solution containing either IFN-β and cpn 10. However, the claim requires that the compounds be in either tablet or capsule form. There is no

guidance in the specification to indicate how one would generate the tablets or the capsule. The prior art also does not teach such formulations. Thus, an undue amount of experimentation would be required to make and use cpn 10 and IFN-β in tablet or capsule form.

Given the breadth of claims 6 and 30 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention of cpn 10 and IFN-β in tablet or capsule form for the treatment of MS. Thus, it would require further guidance for the artisan to predictably be able to make and successfully administer tablet or capsule.

11. No claims are allowable.

12. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 1/06

ROBERT S. LANDSMAN, PH.D
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